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REMARKS

Applicants have concurrently submitted a Request for Continued Examination and a Declaration under 37 C.F.R. § 1.132. Applicants also enclose a photocopy of a PTO-stamped postcard and a photocopy of a PTO-1449 as original filed on October 1, 2001.

Claims 1-5, 11-16 and 18-21 have been amended without prejudice or disclaimer of any subject matter, and without acquiescence to any rejection. These amendments have been made to more particularly describe what Applicants' regard as their invention. Applicants submit that support for the amended claims can be found in the application as originally filed, and, in particular, on pages 9-11 of the specification. Accordingly, no new matter has been added.

I. Information Disclosure Statement

The IDS filed October 1, 2001 has been acknowledged and considered by the Examiner in the Office Action dated June 5, 2003. Office Action, p. 2. The Examiner states the PTO-1449 is missing. *Id.* As indicated by the photocopied, PTO-stamped postcard, a copy of the PTO-1449 was filed on October 1, 2001. For the Examiner's convenience, a copy of the PTO-1449, as originally filed, is provided. Applicants request indication of consideration of the cited documents on the PTO-1449 by the Examiner.

II. Rejections under 35 U.S.C. § 112 first paragraph

Claim 20 is rejected under 35 U.S.C. 112, first paragraph. Office Action, p. 2. The Examiner asserts that (a) the term disease in the claim "encompasses all diseases", (b) "claim 20 ...encompasses the treatment of diseases in general," and (c) U.S. Patents 5,430,047, 5,250,558 and 5,747,303 provide no evidence that "antagonists of neurotensin are useful in treating any specific disease." *Id.* Applicants respectfully traverse this rejection.

With regard to points (a) and (b), the last phrase in claim 20 states that "the disease is chosen from schizophrenia, Parkinson's disease, and Alzheimer's disease." As such, claim 20 is limited to those diseases listed and does not "encompass all diseases" or "the treatment of diseases in general."

With regard to point (c), Applicants previously submitted evidence pursuant to MPEP 609 III.C(3) showing that antagonists of neurotensin are useful in treating the claimed diseases; see, for example, US Pat. No. 5,430,047 at col. 1 lines 20-51, col. 2 lines 1-3, col. 5 lines 60-67, and col. 7 lines 48-65; US Pat. No. 5,250,558 at col. 1 lines 30-40, and col. 2 lines 44-55; US Pat. No. 5,747,303 at col. 5 lines 45-58, col. 6 lines 40-60. Further, Applicants now submit additional evidence pursuant to MPEP 609 III.C(3) showing a link between neurotensin and the claimed diseases. WO 94/10151, p. 25 lines 25-28, p. 28 lines 5-15; Antonelli et al. p. 766 col 2 to p. 767 col. 1. before "Materials and Methods", p. 772 col. 2; Kitabgi abstract, p. 770 first para. in "Neurotensin Dopamine interactions"; Berod & Rostene, p. 96, second para. in

"Conclusions"; Binder et al., abstract, p. 857 col. 1. The above-cited references have been enclosed for the Examiner's convenience.

Moreover, Applicants respectfully submit that the Examiner has not met her burden to establish a *prima facie* case for lack of enablement. To determine enablement, the Examiner is required to assess whether one skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988); *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993); M.P.E.P. § 2164.01. The eight Wands factors (sometimes called the Forman factors) are used to assess undue experimentation, and are delineated in M.P.E.P. § 2164.01(a). *In re Wands*, 858 F.2d 731 *citing In re Forman*, 230 USPQ 546, 547 (Bd. Pat. App & Int 1986); M.P.E.P. § 2164.01(a). To conclude a lack of enablement resulting from undue experimentation, the Examiner must not rely on a single factual determination, but must weigh many factual considerations including the Wands factors. *In re Wands*, 858 F.2d at 737; M.P.E.P. § 2164.01(a). The courts have held that a "considerable amount of experimentation is permissible . . . if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Wands*, 858 F.2d at 737 *citing In re Jackson*, 217 U.S.P.Q. 804, 807 (Bd. App. 1982); See M.P.E.P. § 2164.06.

Here, Applicants respectfully submit that the Examiner has simply asserted that enablement is lacking, but has not discussed any of the Wands factors. Thus, the Examiner's rejection has not met the burden set forth by the courts and as instructed by

the M.P.E.P. For at least these reasons withdrawal of this rejection is earnestly solicited.

Next, the Examiner has rejected claims 1-21 under 35 U.S.C. 112, first paragraph, "because the specification, while being enabling for citrullimycines, does not reasonably provide enablement of derivatives of citrullimycines." Office Action, p. 2. Since Applicants' amendments render this rejection moot, Applicants respectfully request withdrawal of this rejection.

III. Rejections under 35 U.S.C. § 112 second paragraph

The Examiner has rejected claims 1-21 under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Office Action, p. 3. The Examiner alleges "that the 'definition' is not limited to esters, ethers, complexes and adducts," as, in part, disclosed on pages 9-10 of the specification and that "it would take undue amount of experimentation to determine what additional derivatives will result in compounds having the activity of the compounds of formula (I)." *Id.* Since Applicants' amendments render this rejection moot, withdrawal of this rejection is earnestly solicited.

IV. Rejections Under 35 U.S.C. 102 and 103

The Examiner has rejected claim 22 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over *Grabley et al.* (U.S. Patent No. 5,252,472) ("*Grabley*") because differences in the claimed species and the prior art species allegedly cannot be determined. Office Action, pp. 4-5. Applicants respectfully traverse this rejection.

For a claim to be anticipated or obvious, the prior art reference must teach every limitation in the claim. M.P.E.P. § 2131; M.P.E.P. § 2143. Here, the Examiner has compared the species of bacteria in *Grabley* to those instantly claimed, but Applicants respectfully submit that the Examiner has failed to address the differences in the strain of the bacteria. Also, Applicants respectfully submit that the strain of the microorganism has been set forth in claim 22. Applicants believe there is no basis for the Examiner to conclude that the claimed strain is found in *Grabley,* because, *inter alia*, the claimed strain is used to prepare molecules different than those prepared by *Grabley*'s strains. For example, the compounds of formula (I) produced by ST101396 of the instant application (for example, page 3 of Applicants' disclosure) are different from those of formula (I) produced by the different strains of *Grabley* (column 1 lines 35-50). Thus, Applicants respectfully submit that the Examiner has not provided a factual basis to support her conclusion that the instantly claimed strain is anticipated by or obvious over *Grabley* strains.

Moreover, Applicants now present data in the concurrently filed Declaration pursuant to 37 C.F.R. 1.132. These data provide evidence that Applicants' claimed

species, ST 101396, (which is identical to HAG 012114 and is also identified by its deposit number DSM 13309) is neither anticipated by nor obvious over *Grabley*'s strains. The strain comparisons of colony characteristics provided in Table 2 and in the color photographs in Appendix C show, for example, that ST 101396 has different color and formation characteristics compared to those of the *Grabley* strains. Table 3 reveals, for example, that Applicants' claimed strain has a different pattern of carbohydrate utilization than those of the *Grabley* strains. Table 4 exemplifies the differences in the enzymatic activities and the physiological characteristics between Applicants' claimed strain and those of *Grableys'* strains. The fatty acid analyses of the gram positive bacterial cell walls provided in Table 5 demonstrate that (a) Applicants' claimed strain has the characteristic fatty acid profile of the Streptomyces genus, and (b) the cell wall fatty acid composition of Applicants' claimed strain is different from those of *Grableys'* strains. Finally, the ribotyping analysis shows, for example, that the ribosomal RNA genes (as represented by *Pvu*II restriction fragments) of Applicants' claimed strain differs from those of *Grableys*' strains. Since all of these data demonstrate that ST 101396 is a different strain from those identified in *Grabley*, Applicants respectfully submit that the instantly claimed strain, ST 101396, is neither anticipated by nor obvious over *Grabley* strains.

For at least these reasons, Applicants respectfully request withdrawal of these rejections.

V. Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

By: Charles E Van Horn
Charles E. Van Horn
Reg. No. 40,266

Dated: May 20, 2004

Enclosures:

Photocopy of PTO-stamped postcard
PTO-1449 as originally filed on October 1, 2001
U.S. Pat. No. 5,430,047
U.S. Pat No. 5,250,558
U.S. Pat. No. 5,747,303
WO 94/10151
T. Antonelli, et al., Journal of Neuroscience Research, Vol. 70, pp. 766-773 (2002).
P. Kitabgi, Current Opinion in Drug Discovery & Development, Vol. 5, pp. 764-776 (2002).
A. Bérod et al., Current Opinion in Pharmacology, Vol. 2, pp. 93-98 (2002).
E. B. Binder, et al., Biological Psychiatry, Vol. 50, pp. 856-872 (2001).

CPE/CEV/CTR/USD

PLEASE STAMP TO ACKNOWLEDGE RECEIPT OF THE FOLLOWING:

New U.S. Application for:
CITRULLIMYCINES, A PROCESS FOR THEIR PRODUCTION AND THEIR USE AS PHARMACEUTICALS

Inventor(s): Cordula HOPMANN, Michael KURZ, Mark BRONSTRUP; and Joachim WINK

BOX PATENT APPLICATION

1. Check for $776.00
2. Transmittal Letter
3. Spec. 34 pgs. 2 indep. clms. and 22 clms. total
4. Certified copy of European Application No. 00121566.4, filed October 2, 2000
5. Information Disclosure Statement and Information Disclosure Citation, PTO-1449 with documents attached.

OCT 0 1 2001

Dated October 1, 2001

(Due Date: 10/2/01)

Docket No.: 02481.1751
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